

CLAIMS

1. A fat emulsion with which a local anaesthetic is mixed before use, and which comprises propofol, an oily component, and an emulsifier, the fat emulsion further comprising a stabilizer selected from the following (a), (b), (c), or (d):

(a) at least one phospholipid selected from the group consisting of phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, and phosphatidylserine wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid;

(b) at least one phospholipid derivative selected from phosphatidylethanolamines modified with polyalkyleneglycol, wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid;

(c) at least one fatty acid selected from the group consisting of C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acids; or

(d) a mixture of at least two members selected from the above groups (a), (b), and (c), wherein

20 the stabilizer (a), (b), or (c) is present at a concentration of 0.01 to 1 w/v%, 0.01 to 1 w/v%, 0.05 to 5 w/v%, respectively, per the total amount of fat emulsion and local anaesthetic to be mixed therewith before use.

25 2. The fat emulsion according to Claim 1, wherein

(1) propofol is present at a concentration of 0.4 to 5 w/v%,

(2) an oily component is present at a concentration of 2 to 20 w/v%, and

(3) an emulsifier is present at a concentration of 0.4 to

30 5 w/v%, per the total amount of fat emulsion and local anaesthetic to be mixed therewith before use.

35 3. The fat emulsion according to Claim 1, wherein a local anaesthetic is at least one member selected from the group consisting of lidocaine, mepivacaine, bupivacaine, ropivacaine, dibucaine,

procaine, procaine chloride, tetracaine and pharmacologically acceptable acid addition salts thereof.

4. The fat emulsion according to Claim 1, wherein the local anaesthetic is present at a concentration of 0.01 to 1 w/v%, per the total amount of fat emulsion and local anaesthetic to be mixed therewith before use.

5. The fat emulsion according to Claim 1, wherein the stabilizer is at least one phospholipid (a) selected from the group consisting of phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, and phosphatidylserine wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid.

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6. The fat emulsion according to Claim 1, wherein the stabilizer is at least one phospholipid (a) selected from the group consisting of phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, and phosphatidylserine wherein a fatty acid esterified to a glycerol moiety is a C₁₂₋₁₈ linear or branched, saturated or unsaturated fatty acid.

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7. The fat emulsion according to Claim 1, wherein the stabilizer is at least one phospholipid (a) selected from the group consisting of distearoylphosphatidylglycerol, dipalmitoylphosphatidylglycerol, dioleoylphosphatidylglycerol, distearoylphosphatidic acid, dipalmitoylphosphatidic acid, dioleoylphosphatidic acid, distearoylphosphatidylinositol, dipalmitoylphosphatidylinositol, dioleoylphosphatidylinositol, distearoylphosphatidylserine, dipalmitoylphosphatidylserine, and dioleoylphosphatidylserine.

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8. The fat emulsion according to Claim 5, wherein the stabilizer is present at a concentration of 0.03 to 1 w/v%, per the total amount of fat emulsion and local anaesthetic to be mixed therewith

before use.

9. The fat emulsion according to Claim 1, wherein the stabilizer is at least one phospholipid derivative (b) selected from phosphatidylethanolamines modified with polyalkyleneglycol, wherein a fatty acid esterified to a glycerol moiety is a C_{10-22} linear or branched, saturated or unsaturated fatty acid.

10. The fat emulsion according to Claim 1, wherein the stabilizer is at least one phospholipid derivative (b) selected from phosphatidylethanolamines modified with polyalkyleneglycol having an average molecular weight of 1000 to 5000, wherein a fatty acid esterified to a glycerol moiety is a C_{14-18} linear or branched, saturated or unsaturated fatty acid.

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11. The fat emulsion according to Claim 1, wherein the stabilizer is at least one phospholipid derivative (b) selected from the group consisting of distearoylphosphatidylethanolamine-polyethylene glycol 5000, distearoylphosphatidylethanolamine-polyethylene glycol 3000, and distearoylphosphatidylethanolamine-polyethylene glycol 2000.

12. The fat emulsion according to Claim 9, wherein the stabilizer is present at a concentration of 0.1 to 1 w/v%, per the total amount of fat emulsion and local anaesthetic to be mixed therewith before use.

13. The fat emulsion according to Claim 1, wherein the stabilizer is at least one fatty acid (c) selected from the group consisting of C_{10-22} linear or branched, saturated or unsaturated fatty acids.

14. The fat emulsion according to Claim 1, wherein the stabilizer is at least one fatty acid (c) selected from the group consisting of C_{10-20} linear or branched, saturated or unsaturated

acids.

15. The fat emulsion according to Claim 1, wherein the stabilizer is at least one fatty acid (c) selected from the group consisting of decanoic acid, lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, isomyristic acid, isopalmitic acid, and oleic acid.

10 16. The fat emulsion according to Claim 13, wherein the stabilizer is present at a concentration of 0.1 to 5 w/v%, per the total amount of fat emulsion and local anaesthetic to be mixed therewith before use.

15 17. A fat emulsion containing container having a multi-compartment that is divided with a partition in such a manner as to allow the compartments to communicate with one another, which container comprises one compartment containing the fat emulsion according to Claim 1 and another compartment containing a local anaesthetic.

20 18. A pain-relieving fat emulsion comprising propofol, an oily component, an emulsifier, a stabilizer, and a local anaesthetic, wherein the stabilizer is selected from the following (a), (b), (c), or (d):

25 (a) at least one phospholipid selected from the group consisting of phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, and phosphatidylserine wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid;

30 (b) at least one phospholipid derivative selected from phosphatidylethanolamines modified with polyalkyleneglycol, wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid;

35 (c) at least one fatty acid selected from the group consisting of C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acids; or

(d) a mixture of at least two members selected from the above groups (a), (b), and (C), wherein

the stabilizer (a), (b), or (c) is present at a concentration of 0.01 to 1 w/v%, 0.01 to 1 w/v%, and 0.05 to 5 w/v%, respectively, 5 in the fat emulsion.

19. The pain-relieving fat emulsion according to Claim 18, wherein

(1) propofol is present at a concentration of 0.4 to 5 w/v%,

10 (2) an oily component is present at a concentration of 2 to 20 w/v%,

(3) an emulsifier is present at a concentration of 0.4 to 5 w/v%, and

15 (4) a local anaesthetic is present at a concentration of 0.01 to 1 w/v%, in the fat emulsion.

20. The pain-relieving fat emulsion according to Claim 18, wherein a local anaesthetic is at least one member selected from the group consisting of lidocaine, mepivacaine, bupivacaine, ropivacaine, dibucaine, procaine, procaine chloride, tetracaine and pharmacologically acceptable acid addition salts thereof.

21. The pain-relieving fat emulsion according to Claim 18, wherein the stabilizer is at least one phospholipid (a) selected from the group consisting of phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, and phosphatidylserine wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid.

30 22. The pain-relieving fat emulsion according to Claim 18, wherein the stabilizer is at least one phospholipid (a) selected from the group consisting of phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, and phosphatidylserine wherein a fatty acid esterified to a glycerol moiety is a C₁₂₋₁₈ linear or branched, saturated or unsaturated fatty acid.

23. The pain-relieving fat emulsion according to Claim 18, wherein the stabilizer is at least one phospholipid (a) selected from the group consisting of distearoylphosphatidylglycerol, dipalmitoylphosphatidylglycerol, dioleoylphosphatidylglycerol, distearoylphosphatidic acid, dipalmitoylphosphatidic acid, dioleoylphosphatidic acid, distearoylphosphatidylinositol, dipalmitoylphosphatidylinositol, dioleoylphosphatidylinositol, distearoylphosphatidylserine, dipalmitoylphosphatidylserine, and dioleoylphosphatidylserine.

24. The pain-relieving fat emulsion according to Claim 21, wherein the stabilizer is present at a concentration of 0.03 to 1 w/v% in the fat emulsion.

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25. The pain-relieving fat emulsion according to Claim 18, wherein the stabilizer is at least one phospholipid derivative (b) selected from phosphatidylethanolamines modified with polyalkylene-glycol, wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid.

26. The pain-relieving fat emulsion according to Claim 18, wherein the stabilizer is at least one phospholipid derivative (b) selected from phosphatidylethanolamines modified with polyalkylene-glycol having the average molecular weight of 1000 to 5000, wherein a fatty acid esterified to a glycerol moiety is a C₁₄₋₁₈ linear or branched, saturated or unsaturated fatty acid.

27. The pain-relieving fat emulsion according to Claim 18, 30 wherein the stabilizer is at least one phospholipid derivative (b) selected from the group consisting of distearoylphosphatidylethanolamine-polyethylene glycol 5000, distearoylphosphatidylethanolamine-polyethylene glycol 3000, and distearoylphosphatidylethanolamine-polyethylene glycol 2000.

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28. The pain-relieving fat emulsion according to Claim 25, wherein the stabilizer is present at a concentration of 0.1 to 1 w/v% in the fat emulsion.

5 29. The pain-relieving fat emulsion according to Claim 18, wherein the stabilizer is at least one fatty acid (c) selected from the group consisting of C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acids.

10 30. The pain-relieving fat emulsion according to Claim 18, wherein the stabilizer is at least one fatty acid (c) selected from the group consisting of C₁₀₋₂₀ linear or branched, saturated or unsaturated fatty acids.

15 31. The pain-relieving fat emulsion according to Claim 18, wherein the stabilizer is at least one fatty acid (c) selected from the group consisting of oleic acid, isomyristic acid, isopalmitic acid, decanoic acid, lauric acid, myristic acid, palmitic acid, stearic acid, and arachidic acid.

20 32. The pain-relieving fat emulsion according to Claim 29, wherein the stabilizer is present at a concentration of 0.05 to 0.2 w/v% in the fat emulsion.

25 33. A method for manufacturing a pain-relieving fat emulsion, the method comprising:

mixing a local anaesthetic with a fat emulsion comprising propofol, an oily component, an emulsifier, and a stabilizer, wherein the stabilizer is selected from the following (a), (b), (c), or (d):

30 (a) at least one phospholipid selected from the group consisting of phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, and phosphatidylserine wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid;

35 (b) at least one phospholipid derivative selected from

phosphatidylethanolamines modified with polyalkyleneglycol, wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid;

5 (c) at least one fatty acid selected from the group consisting of C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acids; or
(d) a mixture of at least two members selected from the above groups (a), (b), and (c), to thereby obtain a fat emulsion, wherein the stabilizer (a), (b), or (c) is present at a concentration of 0.01 to 1 w/v%, 0.01 to 1 w/v%, and 0.05 to 5 w/v%, respectively, 10 in the fat emulsion.

34. Use of the following stabilizers (a) to (d) for stabilizing a fat emulsion with which a local anaesthetic is mixed before use and which comprises propofol, an oily component, and an emulsifier, or a pain-relieving fat emulsion which comprises propofol, 15 an oily component, an emulsifier, and a local anaesthetic:

(a) at least one phospholipid selected from the group consisting of phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, and phosphatidylserine wherein a fatty acid 20 esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acid;

(b) at least one phospholipid derivative selected from phosphatidylethanolamines modified with polyalkyleneglycol, wherein a fatty acid esterified to a glycerol moiety is a C₁₀₋₂₂ linear or branched, 25 saturated or unsaturated fatty acid;

(c) at least one fatty acid (c) selected from the group consisting of C₁₀₋₂₂ linear or branched, saturated or unsaturated fatty acids; or

(d) a mixture of at least two members selected from the above 30 groups (a), (b), and (c).